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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/822,860	04/13/2004	Koichi Matsuzaki	040176	2658

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EXAMINER	
REDDIG, PETER J	
ART UNIT	**PAPER NUMBER**
1642	
MAIL DATE	**DELIVERY MODE**
09/19/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Advisory Action Before the Filing of an Appeal Brief	**Application No.** 10/822,860	**Applicant(s)** MATSUZAKI ET AL.	
	Examiner Peter J. Reddig	**Art Unit** 1642	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 15 August 2007 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☒ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:
   a) ☒ The period for reply expires 3 months from the mailing date of the final rejection.
   b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

   Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☐ The Notice of Appeal was filed on _____. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. ☐ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
   (a) ☐ They raise new issues that would require further consideration and/or search (see NOTE below);
   (b) ☐ They raise the issue of new matter (see NOTE below);
   (c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
   (d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: _____. (See 37 CFR 1.116 and 41.33(a)).

4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).
5. ☐ Applicant's reply has overcome the following rejection(s): _____.
6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
7. ☒ For purposes of appeal, the proposed amendment(s): a) ☐ will not be entered, or b) ☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.
   The status of the claim(s) is (or will be) as follows:
   Claim(s) allowed: _____.
   Claim(s) objected to: *3,13 and 14*.
   Claim(s) rejected: *1,2,4 and 5*.
   Claim(s) withdrawn from consideration: _____.

AFFIDAVIT OR OTHER EVIDENCE

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).
9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).
10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because: See Continuation Sheet.
12. ☐ Note the attached Information Disclosure Statement(s). (PTO/SB/08) Paper No(s). _____
13. ☐ Other: _____.

SUSAN UNGAR, PH.D
PRIMARY EXAMINER

Continuation of 11. does NOT place the application in condition for allowance because:
Claim 1, 2, 4 and 5 remain rejected under 35 USC 103(a) for the reasons previoulsy set forth in the Office Action of May 17, 2007, section 9, pages 5-13.

Applicants argue that the polyclonal antibody of the present invention is characterized in that it does not recognize the phosphorylation of the C-terminal region, but recognizes the phosphorylation of the linker region. (That is, the recitation "specific for a phosphorylated linker region .... "in claims 1 and 2). None of the references cited teaches or suggests any antibody capable of selectively recognizing only Smad's that are phosphorylated at the linker region, because the conventional antibodies just recognize the phosphorylation itself and cannot distinguish between the phosphorylation of the C-terminal region and that of the linker region. The present polyclonal antibody can specifically recognize the phosphorylation of the linker region and consequently can be useful for selectively detecting diseases pathologically associated with the phosphorylation of the linker region.

Applicants' arguments have been carefully considered, but have not been found persuasive. Applicant appears to be arguing that specificity is equivalent to selectivity however, those of ordinary skill in the art recognize that the specificity of antibody binding is related to the epitope to which an antibody binds and therefore a "specific' antibody will bind to any protein or portion thereof that contains that eptiope. On the other hand selectivity of an antibody is understood by those of ordinary skill in the art to be the process wherein an antibody will bind to only a single protein comprising the epitope to which the antibody is directed. Applicants are arguing limitations not found in the claims, i.e. specifically an antibody characterized in that it does not recognize the phosphorylation of the C-terminal region, but recognize the phosphorylation of the linker region and antibodies that selectivey recognize only Smad's that are phosphrylated at the linker region.

Applicants argue that where an antigen is known, general technology for obtaining monoclonal antibodies as well as polyclonal antibodies to such an antigen has been established in the art. However, where there are a great number of antigenic candidates, there would be as well a great number of possible choices as to which antigen is selected to obtain the desired antibody. Such a choice is not obvious and rather difficult if no suggestion is provided. Accordingly, it is not obvious even to one of ordinary skill in the art to obtain an antibody capable of recognizing only Smad proteins which are phosphorylated at the linker region.

Applicants' arguments have been carefully considered, but have not been found persuasive. As previously set forth in the Office action of May 17, 2007, pages 4-13, Kretzschmar et al. identify phosphorylations in the linker region of SMAD2 and/or 3 and provide the motivation for making antibodies to this region given that the phosphorylations are regulated by a known oncogene, Ras, and the importance of understanding the cellular mechanisms related to cancer.

Applicants argue that the importance of the phosphorylation of the linker region was not recognized before filing of the above-identified application. Under the circumstances, the present inventors found that the phosphorylation of the linker region is increased with the development of hepatic fibrosis and canceration and consequently associated with the hepatic fibrosis and canceration. Based on this finding, the present inventors found for the first time the fact that only the phosphorylation of the linker region is significant for the detection of those diseases.

Applicants' arguments have been carefully considered, but have not been found persuasive. As set forth above and previously, the importance of the phosphorylation of the linker region was recognized by Kretzschmar et al. prior to the filing of the application. Although the phosphorylation of the linker region is significant for the detection of hepatic fibrosis and canceration by the claimed antibody, prima facie obviousness is not rebutted by merely recognizing additional advantages of the claimed product, see MPEP 2145 (II).

Applicants argue that they have not amended claims 3, 13 and 14 to be independent at this time. Applicants argue for reconsideration of the objection to these claims in view of the above arguments concerning the rejection of base claim 2.

Applicants arguments have been considered, but have not been found persusasive because base claim 2 remains rejected and thus claims 3, 13, and 14 remain objected to for the reasons previously set forth.

Applicant's arguments have not been found persuasive and claims 1, 2, 4 and 5 remain rejected and claims 3, 13, and 14 remain objected to.